

Appln No. 10/510,617
Amdt date August 17, 2007
Reply to Office action of April 17, 2007.

REMARKS

Claims 11-18 are pending in the application. In the Office action, the Examiner withdrew claims 17 and 18 from consideration as being directed to a non-elected invention; rejected claims 13 and 16 for failing to meet the written description requirement of 35 U.S. C. § 112, first paragraph, as well as for being indefinite (35 U.S. C. § 112, second paragraph); and rejected claims 11-16 under 35 U.S. C. § 103 (a) as being obvious in view of a combination of multiple references. Applicant respectfully traverses the rejections and requests reconsideration.

Withdrawn Claims

Applicant has cancelled claims 17 and 18 without prejudice.

Rejections Based on Written Description

Claims 13 and 16 stand rejected as purportedly failing to meet the written description requirement. Applicant submits that the claims (as presently amended, where appropriate) find full support in the specification of the application. In this regard, the Examiner is reminded that the original claims are considered part of the specification. *Hyatt v. Boone*, 146 F.3d 1348, 1352, 47 USPQ 2d. 1128, 1130 (Fed. Cir. 1998) ("The claims as filed are part of the specification, and may provide or contribute to compliance with § 112. See *Northern Telecom, Inc. v. Data Point Corp.*, 908 F 2d. 931, 938, 15 USPQ 2d. 1321, 1326 (Fed. Cir. 1990) (The original claims are part of the patent specification...") (Additional citations omitted).

For the Examiner's convenience, the following table is provided to illustrate where support for various claim limitations can be found. All references are to the English translation of the specification. Copies of selected pages from the specification, including the original claims, are attached, with line numbering added for clarification.

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Limitation

"providing"

"optionally crushing the Lycium barbarum"

"providing and optionally crushing the Cuscuta chinensis Lam"

"optionally combining two or more of the herbs"

"extracting . . .in a 0-95% alcohol mixture"

"at a temperature in the range of 1 to 98 °C"

"1 to 4 times"

"to form one or more extracted liquor(s)alcohol mixtures"

"optionally mixing the extracted liquor(s)/alcohol mixtures"

Support

Orig. claim 5, l.4 ("The raw herbs are weighed . . ."); Spec., p. 7, l. 6¹

Orig. claim 5, l. 6-7 ("including raw material or crushed powder of Lycium barbarum L. . ."; Spec., p. 7, l. 8-9

Orig. claim 5, l. 6-7 ("including raw material or crushed powder of Lycium barbarum L. and Cuscuta chinensis Lam . . ."; Spec., p. 7, l. 8-9

This limitation is moot in view of the present amendment

Orig. claim 5, l. 4-8 (extraction in ethanol); Spec. p. 7, l. 9-11 ("The 4 kinds of herbs are extracted in the 0~95% alcohol . . ."

Orig. cl. 5, l. 8; Spec., p. 7, l. 10

Orig. cl. 5, l. 9; Spec., p. 7, l. 10

Orig. cl. 5, l. 8-10; Spec., p. 7, l. 9-11

Orig. cl. 5, l. 9-10; Spec., p. 7, l. 11

¹ Obviously, the herbs cannot be weighed unless they are present, that is available. The word "providing" simply means making the herbs available for subsequent processing, e.g., cutting, crushing, mixing, extracting, etc.

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"recovering the extracted liquor(s)/alcohol mixtures"	Spec., p. 7, l. 11-12
"condensing, drying, and smashing the extracted liquor(s) to form extracted herb powders"	Spec., p. 7, l. 11-12
"mixing the extracted herb powders uniformly or proportionally to form a pharmaceutical mixture"	Orig. cl. 5, l. 11-12; Spec., p. 7, l. 12-13

Additional limitations, recited in claim 16, are similarly supported by the specification, including the original claims.

<u>Limitation</u>	<u>Support</u>
"extracting . . . a decoction fluid"	Spec., p. 6, l. 17-23 (decoction in water)

Other limitations questioned by the Examiner are now moot in view of the present amendment, e.g., cutting into "small" pieces; crushing Lycium barbarum L to a "coarse" powder; mixing the "extract powder," etc.

Since claims 13 and 16 are, in fact, supported by the specification (including the original claims), the rejections under 35 U.S. C. § 112, first paragraph, should be withdrawn.

Rejection Based on Indefiniteness

The rejections of claims 13 and 16 under 35 U.S. C. § 112, 2nd paragraph, have been obviated by the present amendments to those claims. Note also that claim 14 has been amended to refer to "specific gravity."

Rejection of the Claims Based on Obviousness

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Claims 11-16 stand rejected as purportedly being obvious in view of Xu et al., taken in combination with 7 or 8 additional references. The basic thrust of the Examiner's position is found on pages 22 and 23 of the Office action:

[S]ince each of the references teach that *Tripterygium hypoglauicum*, *Epimedium brevicornum*, *Lycium barbarum*, and *Cuscuta chinensis* are effective ingredients in compositions for treating rheumatism, it would have been obvious to combine these plants with the expectation that such a combination would be effective in treating rheumatism. Thus, combining them flows logically from their having been individually taught in [the] prior art.

Applicant disagrees. The Examiner has not found references that show the use of one or two of the four herbs used in Applicant's invention to prepare a pharmaceutical for treating rheumatism, and then combined them based on the idea that "combining them flows logically from their having been individually taught in the prior art." To the contrary, the Examiner has selected bits and pieces from disparate disclosures while ignoring other key ingredients taught by the references, to arrive at the present invention through an improper hindsight reconstruction.

For example, the primary reference (Xu et al.) teaches a medicine made with centipede(!), *Tripterygium hypoglauicum* Hutch, giant typhonium herb, ground beetle(!), rootbark of Chinese Hydrangeavike, root of fourstamen stephamia, root of Mongolian milkvetch, flower of Chinese Azalea, Chinese Taxillus herb, fruit of Barbary Wolfberry (purportedly synonymous with *Lycium barbarum*), and root of ural licorice. Similarly, Xiong et al. does not merely teach the use of *Epimedium Brevicornum* and ripe fruit of Barbary Wolfberry but, in fact, discloses a "snake spirit" that includes, snake meat(!), radix notoginseng, and desert living cistanche. The Examiner has pointed to nothing that would direct the skilled person to make a medicinal formulation containing the four herbs *Tripterygium hypoglauicum*, *Epimedium*

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brevicornum, Lycium barbarum, and Cuscuta chinensis, present in the recited amounts, that is both effective and safe.

Efficacy and safety are important features of the claimed formulations and methods of making same, as pointed out in the first paragraph of page 3 of the application. Although there are vast numbers of Chinese herbal medicines and treatments, the prior art suffers from poor or mixed efficacy, often deleterious side effects, and sometimes difficult administration, as pointed out in the bottom paragraph of page 2 of the application. In contrast, the present invention provides an effective treatment for rheumatism characterized by the combination of the four herbs recited in claims 11 and 12, with the various weight percentages as recited. No combination of references cited by the Examiner teaches, suggests, or otherwise leads to the present invention. Without the present application as a roadmap, the skilled person could not take Xu et al. and Xiong et al. and select the four herbs recited in Applicant's claims while ignoring the other, potentially toxic ingredients disclosed in the references.

The application as filed (pages 8-49) is replete with evidence that the claimed formulations are effective in treating rheumatism. Tests on mice showed that it could inhibit primary and secondary adjuvant arthritis (AA), delayed hypersensitivity (DTH) in the ear caused by DNFB, hemolysin antibody production and the activity of IL-1, IL-2, IL-6, and TNF in macrophages and splenocytes, as well as lymphocyte transformation induced by ConA, and could also inhibit CD4 and CD8 cells without affecting the CD4/CD8 ratio much. The medicine had a remarkable anti-inflammatory action.

In rebuttal to the Examiner's assertion that it is logical to combine any known treatment for rheumatism with another treatment for rheumatism, Applicant has attached a summary of tests conducted by the inventor, Deng WenLong, who graduated from West China University of Medical Sciences majoring in Pharmacology in 1963, who has committed himself to R&D in the pharmacological field since 1983, who directs the Chinese Pharmacology Society, and who has published more than 100 papers, and various academic monographs. Table 1 presents the results

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of tests in which atrophy of the testicles, thymus, and spleen was induced by oral administration of *Tripterygium hypoglauicum* (Levl.) Hutch, followed by treatment with (a) *Epimedium brevicornum Maxim.*, *Lycium barbarum*, and *Cuscuta chinensis Lam.* (collectively denoted "The herbs compound 1") plus additional *Tripterygium hypoglauicum* (Levl.) Hutch, or (b) *Lycium barbarum* plus *Cuscuta chinensis Lam.* (collectively denoted "The herbs compound 2") and additional *Tripterygium hypoglauicum* (Levl.) Hutch. In other words, treatment (a) corresponds to the four-herb formulation presently claimed.

Whereas administration of *Tripterygium hypoglauicum* (Levl.) Hutch induced tissue atrophy, the co-administration of the four herbs recited in Applicant's claims substantially alleviated injury to the testicles (evidence is also provided for the thymus and spleen). The absence of *Epimedium brevicornum Maxim* in treatment (b), however, resulted in far less recovery from injury. This shows that it is not, as the Examiner suggests, a simple matter of willy nilly combining various herbal formulations known to treat rheumatism, as certain herbs, taken by themselves (e.g., *Tripterygium hypoglauicum* (Levl.) Hutch), can cause serious side effects, and not all combinations of anti-rheumatism treatments will achieve the desired balance of efficacy and low toxicity.

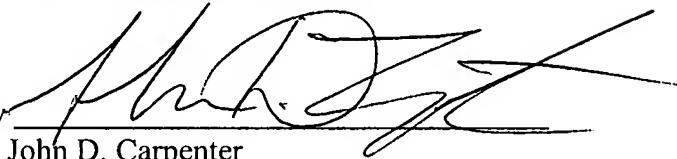
Applicant submits that the Examiner has not presented a *prima facie* case of obviousness, as there is nothing in the cited art that would lead the skilled person to select *Tripterygium hypoglauicum* (Levl.) Hutch, *Epimedium brevicornum Maxim.*, *Lycium barbarum*, and *Cuscuta chinensis Lam.* as an effective and safe formulation for treating rheumatism. The argument that such a combination flows logically from various references that teach the use of one or more of the herbs (typically in combination with numerous other compounds) as a treatment for rheumatism is effectively rebutted by the evidence that certain herbs have individual toxic effects, and the wrong combination of herbs cannot adequately counter the negative side effects. This is potent evidence of unexpected results obtained by the present invention.

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Accordingly, Applicant requests reversal of the rejections and a notice of allowance.

Respectfully submitted,

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1. Choosing 70 mice , 18-22g , the number of male and that of female are equal, they are separated into seven groups at random , and drenched drug one time everyday according to Table 1 for two weeks , and dissecting them at term , weighing testicle, thymus and spleen , the result is as follows :

Table 1 the herbs compound's effect on white mice' atrophia testiculi induced by Tripterygium hypoglaucum (Levl.) Hutch. ($\bar{X} \pm SD$, mg/100g)

Comparing to the control group *P<0.05 , **P<0.01

group	dose (g/kg)	testicle	thymus	spleen
Control		486±44*	125±32**	202±53
Tripterygium hypoglaucum (Levl.) Hutch.	20	344±94	55±24	210±60
The herbs compound 1+ Tripterygium hypoglaucum (Levl.) Hutch.	20+20	443±45*	112±55*	237±65
The herbs compound 2+ Tripterygium hypoglaucum (Levl.) Hutch.	20+20	371±62	88±45	198±65
cyclophosphamide	0.02	262±42**	44±25**	165±45

The herbs compound 1: Epimedium brevicornum Maxim.+Lycium barbarum L.+Cuscuta chinensis Lam.

The herbs compound 2: Lycium barbarum L.+Cuscuta chinensis Lam.

From table 1 , we can see that the compound of Epimedium brevicornum Maxim., Lycium barbarum L., Cuscuta chinensis Lam. and Tripterygium hypoglaucum (Levl.) Hutch. can alleviate the injury of testicle from

Tripterygium hypoglaucum (Levl.) Hutch.

2. Choosing 70 mice , 18-22g ,the number of male and that of female are equal, they are separated into seven groups at random , and drenched drug one time everyday for seven days , from the day of drenching drug each mice acquires immunity with 0.2ml 5% chicken red blood cell suspension .When the experiment is due , fetching blood from postorbital venous plexus of each mouse , and measuring HC_{50} according to the measures ,the result is in Table 2. Then testing with another 70 mice by the same methods, while the experiment drugs are different, the result is in Table 3.

Table 2 the effect of *Tripterygium hypoglaucum* (Levl.) Hutch., *Epimedium brevicornum* Maxim., *Lycium barbarum* L. and *Cuscuta chinensis* Lam. on the mice creating hemolysin

Group	dose (g/Ig)	HC_{50}
control		282 ± 38
<i>Tripterygium hypoglaucum</i> (Levl.) Hutch.	5	233 ± 25
<i>Tripterygium hypoglaucum</i> (Levl.) Hutch.	10	203 ± 21
<i>Tripterygium hypoglaucum</i> (Levl.) Hutch.	20	179 ± 22
<i>Epimedium brevicornum</i> Maxim.	20	256 ± 42
<i>Lycium barbarum</i> L.	10	315 ± 34
<i>Cuscuta chinensis</i> Lam.	10	296 ± 32

Table 3 the effect of different compatibility of *Tripterygium hypoglaucum* (Levl.) Hutch. on the mice creating hemolysin

group	dose (g/Ig)	HC_{50}

control		263±42
Tripterygium hypoglauicum (Levl.) Hutch.	20	168±12
Tripterygium hypoglauicum (Levl.) Hutch.+ Epimedium brevicornum Maxim.	20+20	142±36
Tripterygium hypoglauicum (Levl.) Hutch.+ Lycium barbarum L.	20+10	173±35
Tripterygium hypoglauicum (Levl.) Hutch.+ Cuscuta chinensis Lam.	20+10	185±28
Tripterygium hypoglauicum (Levl.) Hutch.+ Epimedium brevicornum Maxim.+ Lycium barbarum L.+ Cuscuta chinensis Lam.	20+20+10+10	79±16
Tripterygium hypoglauicum (Levl.) Hutch.+ Epimedium brevicornum Maxim.+ Lycium barbarum L.+ Cuscuta chinensis Lam.	10+20+10+10	122±22

From Table 2 and Table 3, it can be seen that: Tripterygium hypoglauicum (Levl.) Hutch can restrain the generation of antibody, Epimedium brevicornum Maxim., Lycium barbarum L. and Cuscuta chinensis Lam cannot affect the generation of antibody obviously, but the combination of Epimedium brevicornum Maxim., Lycium barbarum L., Cuscuta chinensis Lam. and Tripterygium hypoglauicum (Levl.) Hutch. can increase the immunological suppression effect highly.